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10/565,669	01/24/2006	Tomoharu Kiyuna	Q92767	2893

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EXAMINER	
CLOW, LORI A	
ART UNIT	PAPER NUMBER
1631	

NOTIFICATION DATE	DELIVERY MODE
12/17/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/565,669	KIYUNA ET AL.	
	Examiner	Art Unit	
	LORI A. CLOW	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,17 and 23-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,17 and 23-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/24/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' response, filed 24 Se[tember 2009, has been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-15, 17, and 23-29 are currently pending and under exam herein. Claims 16 and 18-22 have been cancelled.

Information Disclosure Statement

The Information Disclosure Statement filed 24 January 2006 has been considered in full. A signed copy of PTO form 1449 is included with this Office Action. It is noted that this IDS was previously considered in full and that the line-through was a typographical error.

Claim Objections

The outstanding claim objections have been withdrawn in view of the claim amendments.

Claim Rejections - 35 USC § 101-Non-statutory Subject Matter

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-15, 17, and 23-29 remain rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter, for the reasons set forth in the previous Office Action and re-iterated below.

Claims 1-15, 17, and 23-29 are drawn to a method of measuring a chromosome territory, the method detecting a difference in state between a plurality of cells containing a chromosome territory by measuring a desired area of said cells in information of a plurality of images comprising extracting data from images and classifying images into classes.

In accord with the decision in *In re Bilski*, a claim to a process or method must meet the machine-or-transformation test in order to be eligible under 35 USC 101 as statutory subject matter (*In re Bilski*, 545 F.3d 943, 88 USPQ2d 1385 (Federal Circuit, 2008). In other words, the prohibition on patenting abstract ideas has two distinct aspects: (1) when an abstract concept has no claimed practical application, it is not patentable; (2) while an abstract concept may have a practical application, a claim reciting an algorithm or abstract idea can state statutory subject matter only if it is embodied in, operates on, transforms, or otherwise is tied to another class of statutory subject matter under 35 U.S.C. §101 (i.e. a machine, manufacture, or composition of matter). (*Gottschalk v. Benson*, 409 U.S. 63, 175 USPQ 673, 1972), as clarified in *In re Bilski*, 545 F.3d 943, 88 USPQ2d 1385 (Federal Circuit, 2008) the test for a method claim is whether the claimed method is (1) tied to a particular machine or apparatus or (2) transforms a particular article to a different state or thing.

In the instant case, the method claims are not so tied to another statutory class of invention because the method steps that are critical to the invention are "not tied to any

particular apparatus or **machine**" and therefore do not meet the machine-or-transformation test as set forth in *In re Bilski* 545 F.3d 943, 88 USPQ2d 1385 (Federal Circuit, 2008).

Response to Applicant's Arguments

The Examiner further respectfully disagrees with the characterization that In re Bilski does not apply to Applicant's invention. The Examiner directs Applicant to the Interim Examination Instructions for Evaluating Subject Matter Eligibility Under 35 USC 101 that can be found at http://www.uspto.gov/web/offices/pac/dapp/opla/2009-08 25_interim_101_instructions.pdf. The Examination Instructions clearly state that a claim to a process, of which is instantly claimed, must pass the machine-or-transformation test which ensures that the process is limited to a particular practical application. It is maintained that in the instant case, the method claims do not meet such requirement and therefore remain rejected.

While it is appreciate that Judge Michel provided an opinion on the *Bilski* decision, as submitted by Applicant, this has no bearing on the examination of process claims as decided by the CAFC and as directed by the instructions recited above.

Claim Rejections - 35 USC § 112-2nd paragraph

The outstanding rejections under 35 USC 112, 2nd paragraph have been withdrawn in view of the claim amendments.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-15, 17, and 23-29 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Parada et al. (Trends in Cell Biology (2002) Vol. 12, No. 9, pages 425-432; PTO form 1449 reference) in view of 7,136,540 (Kiyuna), for the reasons set forth in the previous Office Action and re-iterated below.

The instant claims are drawn to a method of measuring a chromosome territory, the method detecting a difference in state between a plurality of cells containing a chromosome territory by measuring a desired area in images having an attribute value. The method comprises extracting a chromosome territory from an image, standardizing and quantifying, detecting a difference in state between cells and classifying said images into classes wherein classifying includes setting values for an attribute parameter indicating an attribute value of each of said classes and for a mixture ratio. Membership probabilities and evaluation functions are calculated to represent a goodness estimation based on said membership probability and a mixture probability distribution and classifying based on fitting or not fitting a predetermined condition.

In regard to claims 1, 5, and 11, Parada et al. teach that chromosomes occupy distinct territories in the interphase cell nucleus (abstract). Recent advances in microscopy allow the routine visualization of said chromosomes in the interphase nucleus and visualization of chromosome territories (see Section 1. Chromosome Territories; Figure 3). Parada et al. also teach that by observing chromosomal territories and positioning, functional roles may be elucidated (see section 5.). These observations in positioning also are extremely useful in areas of cancer detection and tissue specific arrangement of chromosomes, as is taught in Section 6.

Parada et al. do not teach the specifics of the statistical imaging techniques used in the microscopic analysis, however, Kiyuna does teach a method and system of picture region extraction in which a picture region is extracted based on class membership probability (abstract). Specifically, Kiyuna teaches the parameters of claims 1-15 and 17, as follows:

"first step in which the data space constituted by all the attribute values that may be taken by the each pixel on the picture is divided into subspaces with a given resolution, a 65 collection of pixels, each of which takes an attribute value in the each subspace, the average of the attribute

values of the pixels, and the number of the pixels are retained to constitute a coarse-grained space,
a second step in which the number of pixels in the each subspace is divided by the total number of pixels contained in the picture to calculate the coarse-grained empirical probability distribution in the coarse-grained data space,
a third step in which the class parameter, the number of the classes, and the mixture ratio of the classes, which define the attributes of the each class, are initialized,
a fourth step in which a conditional probability distribution under the class being specified is calculated from the class parameter that defines the attributes of the each class, and the conditional probability distribution under the class being specified is averaged within the each subspace to calculate a coarse-grained conditional probability distribution,
a fifth step in which a class membership probability, which is the probability that each pixel constituting the picture belongs to the each class, is calculated by multiplying the class mixture ratio by the coarse-grained conditional probability distribution,
a sixth step in which the class parameter and the class mixture ratio are updated so as to increase an evaluation function,
a seventh step in which a coarse-grained log-likelihood is calculated as the evaluation function using the coarse-grained conditional probability distribution,
an eighth step in which whether the evaluation function satisfies a given termination condition or not is examined, and
a ninth step in which after the evaluation function satisfies the given termination condition, the class parameter and the class mixture ratio are retained, and the region each pixel belongs to is determined based on the class membership probability to extract the desired region,
the fourth, fifth, sixth, seventh and eighth steps being repeated until the evaluation function satisfies the given condition.
In the preferred construction, in the fourth step, when calculating the coarse-grained conditional probability distribution, the average value of the data included in the each subspace is calculated, and the average value is used to calculate the coarse-grained conditional probability distribution in the each subspace.
In another preferred construction, the picture region extraction method further comprises a tenth step in which whether the coarse-grained resolution is equal to the original resolution or not is examined when the evaluation function satisfies the given terminal condition in the eighth step, and an eleventh step in which the resolution of the subspace is reverted to the original resolution if the resolution of the coarse-graining is not the original resolution,
the fourth, fifth, sixth, seventh, and eighth steps being repeated until the given condition is satisfied, using the class parameter and the class mixture ratio that are retained in the ninth step as the initial value in the third step.
In another preferred construction, in the fourth step, when calculating the coarse-grained conditional probability distribution, the average value of the data included in the each subspace is calculated, and the average value is used to calculate the coarse-grained conditional probability distribution in the each subspace,
which comprises a tenth step in which whether the coarse-grained resolution is equal to the original resolution or not is examined when the evaluation function satisfies the given terminal condition in the eighth step, and an eleventh step in which the resolution of the subspace is

reverted to the original resolution if the resolution of the coarse-graining is not the original resolution,
the fourth, fifth, sixth, seventh, and eighth steps being repeated until the given condition is satisfied, using the class 5 parameter and the class mixture ratio that are retained in the ninth step as the initial value in the third step.
In another preferred construction, in the ninth step, the estimated class mixture ratio is multiplied by the total number of pixels constituting the picture to calculate the 10 number of pixels belonging to the each class, and the pixels in decreasing order of the class membership probability are selected to determine the pixels belonging to the each class.
In another preferred construction, in the seventh step, AIC is used as the evaluation function, and the parameter is 15 changed so that the evaluation function may be decreased in the sixth step.
In another preferred construction, in the seventh step, MDL is used as the evaluation function, and the parameter is changed so that the evaluation function may be decreased 20 in the sixth step.
In another preferred construction, in the seventh step, Structural Risk is used as the evaluation function, and the parameter is changed so that the evaluation function may be decreased in the sixth step. 25
In another preferred construction, the third step comprises a first step in which a neighborhood radius which defines whether the each subspace is close to one another, and the number of the classes are set, a second step in which the representative value of each subspace is set for each sub- 30 space, a third step in which the collection of the classification target subspace is set, a fourth step in which the subspace with the highest coarse-grained empirical probability is selected among the classification target subspaces, a fifth step in which all the subspaces having a representative 35 value whose distance to the representative value of the subspace with the highest coarse-grained empirical probability falls within the neighborhood radius are selected as a neighborhood collection, a sixth step in which whether the shortest distance between the representative value of the 40, subspace included in a class for which classification has already been completed, and the representative value of the subspace included in the neighborhood collection is larger than the neighborhood radius is examined, a seventh step in which the neighborhood collection is defined as a new class 45 if the shortest distance between the representative value of the subspace included in a class for which classification has already been completed and the representative value of the subspace included in the neighborhood collection is larger than the neighborhood radius, the neighborhood collection is 50 deleted from the classification target subspace, and the fourth steps and later are repeated, an eighth step in which if the shortest distance is equal to or shorter than the neighborhood radius, the neighborhood collection is added to the classified classes, and the neighborhood collection is 55 deleted from the classification target subspace, a ninth step in which whether the classification target subspace is an empty collection or not is examined, a tenth step in which if the classification target subspace is not an empty collection, the fourth step and later are repeated, and if the classification 60 target subspace is an empty collection, whether the number of classes for which classification has already been completed is equal to a given number or more is examined, an eleventh step in which if the number of classes for which classification has already been completed is fewer than the 65 given number, the neighborhood radius is diminished, and the third step and later are repeated, a twelfth step in which

if the classification target subspace is an empty collection and the number of classified classes is greater than a given number, the class parameter is calculated within each class and taken as the initial value of the class parameter, also, the ratio of the number of subspaces included in each class is taken as the initial value of the class mixture ratio." (beginning column 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have used the imaging techniques of Kiyuna with the microscopic evaluation of chromosome territories, as taught by Parada et al. One would have had a reasonable expectation of success in doing so, as imaging statistical techniques are well know in the art for evaluation of cell and cellular structures and Parada et al. is a generalized method for extracting a target object region from image data.

Response to Applicant's Arguments

Applicant argues that "Parada et al. make claer that as of the references' publication date the state of the art of chromosome territory measurement is highly unpredictable, nascent and unrealized". Applicant cites lines from the reference to support such a statement.

This is not persuasive. Parada et al. teach that the "recent advances in microscopy now allow for the routine visualization of chromosomes in the interphase nucleus" (page 425, column 1, paragraph 2) and that "the territorial organization of chromosomes in interphase cells was originally proposed by Rabl and Boveri more than a century ago, and was confirmed in the 1980s by Cremer and clooeagues using elegant ultraviolet-laser microirradiation experiments" (page 425, column 2, paragraph 1). Further, Parada et al. teach that "chromosome territories can now be visualized directly by in situ hybridization using fluorescently labeled probes addressed to single chromosomes: (page 425, column 2, paragraph2). Therefore, Parada et al. teach that chromosome visualization was state of the art at the time of the publication of Parada et al. The

limitations thatApplicant seem to be arguing are not present in the instant claims and Applicant is reminded that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Further, it is Kiyun et al that are relied upon to teach the statistical measurements of the instant claims, as was stated in the previous Office Action. Kiyuna is directed to statistical imaging techniques and extracting a target object region from image data, as is instantly claimed.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

December 15, 2009
/Lori A. Clow, Ph.D./
Primary Patent Examiner
Art Unit 1631